THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appellant(s):	Boza et al.
Appl. No.:	09/646,748
Conf. No.:	7778
Filed:	December 11, 2000
Title:	METHOD FOR PROVIDING GLUTAMINE
Art Unit:	1654
Examiner:	A. Mohamed
Docket No.:	112701-036

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPELLANTS' APPEAL BRIEF

Sir:

Appellants submit this Appeal Brief in support of the Notice of Appeal filed on March 13, 2007. This Appeal is taken from the Final Rejection in the Office Action dated October 16, 2006.

I. REAL PARTY IN INTEREST

The real party in interest for the above-identified patent application on Appeal is Nestec, Ltd. by virtue of an Assignment dated December 11, 2000 and recorded at reel 011372, frame 0309 in the United States Patent and Trademark Office.

II. RELATED APPEALS AND INTERFERENCES

Appellants' legal representative and the Assignee of the above-identified patent application do not know of any prior or pending appeals, interferences or judicial proceedings which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision with respect to the above-identified Appeal.

III. STATUS OF CLAIMS

Claims 1-16 are pending in the above-identified patent application. Claims 1-16 stand rejected. Therefore, Claims 1-16 are being appealed in this Brief. A copy of the appealed claims is included in the Claims Appendix.

IV. STATUS OF AMENDMENTS

A final Office Action was mailed on October 16, 2006. Appellants filed a response to the final Office Action on January 3, 2007 with no amendments to the claims. An Advisory Action was mailed on February 6, 2007. In the Advisory Action, the response was considered but the Examiner maintained the previous rejection. Appellants filed a Notice of Appeal on March 13, 2007. A copy of the final Office Action and the Advisory Action are attached as Exhibit A and Exhibit B, respectively, in the Evidence Appendix.

V. SUMMARY OF CLAIMED SUBJECT MATTER

A summary of the invention by way of reference to the specification and/or figures for each of the independent claims is provided as follows:

Independent Claim 1 is directed to a method for increasing plasma glutamine concentration in a stressed mammal (page 1, lines 3-7), the method comprising the step of administering to the stressed mammal a nutritional composition (page 6, lines 17-24) including a protein source having at least 80% by weight of a component selected from the group consisting of whey protein (page 2, line 35 to page 3, line 11; page 3, line 34 to page 4, line 23; page 4, lines 24-35), and a protein mixture which simulates the amino acid profile of whey protein consisting of approximately 80% to about 90% by weight of casein, approximately 0.5% to about 2% by weight of isoleucine, about 2% to about 8% by weight of leucine, about 1% to about 5% by weight of cysteine, and about 1% to about 5% by weight of lysine (page 3, line 34 to page 4, line 23).

Independent Claim 2 is directed to a method for increasing muscle glutamine concentrations in a mammal (page 3, lines 16-20), the method comprising the step of administering to the mammal a nutritional composition (page 6, lines 17-24) including a protein source having at least 80% by weight of a component selected from the group consisting of whey protein (page 3, lines 16-20; page 3, line 34 to page 4, line 23; page 4, lines 24-35), and a protein mixture which simulates the amino acid profile of whey protein consisting of approximately 80% to about 90% by weight of casein, approximately 0.5% to about 2% by weight of isoleucine, about 2% to about 8% by weight of leucine, about 1% to about 5% by weight of cysteine, and about 1% to about 5% by weight of lysine (page 3, line 34 to page 4, line 23).

Independent Claim 3 is directed to a method for providing glutamine to a mammal suffering from injured, diseased or under-developed intestines (page 3, lines 21-26), the method comprising the step of administering to the mammal a nutritional composition (page 6, lines 17-24) including a protein source having at least 80% by weight of a component selected from the group consisting of whey protein (page 3, line 34 to page 4, line 23; page 4, lines 24-35), and protein mixture which simulates the amino acid profile of whey protein consisting of approximately 80% to about 90% by weight of casein, approximately 0.5% to about 2% by weight of isoleucine, about 2% to about 8% by weight of leucine, about 1% to about 5% by

weight of cysteine, and about 1% to about 5% by weight of lysine (page 3, line 34 to page 4, line 23).

Although specification citations are given in accordance with C.F.R. 1.192(c), these reference numerals and citations are merely examples of where support may be found in the specification for the terms used in this section of the Brief. There is no intention to suggest in any way that the terms of the claims are limited to the examples in the specification. As demonstrated by the references numerals and citations, the claims are fully supported by the specification as required by law. However, it is improper under the law to read limitations from the specification into the claims. Pointing out specification support for the claim terminology as is done here to comply with rule 1.192(c) does not in any way limit the scope of the claims to those examples from which they find support. Nor does this exercise provide a mechanism for circumventing the law precluding reading limitations into the claims from the specification. In short, the references numerals and specification citations are not to be construed as claim limitations or in any way used to limit the scope of the claims.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. Claims 1-2 and 6 are rejected under 35 U.S.C. §102(b) as being anticipated by the publication of 100% Whey Proteins 5 lbs by Optimum Nutrition ("*Optimum Nutrition*"). A copy of *Optimum Nutrition* is attached herewith as Exhibit C in the Evidence Appendix.

2. Claims 1-16 are rejected under 35 U.S.C. §103(a) as being unpatentable over *Optimum Nutrition* in view of U.S. Patent No. 5,849,335 to Ballevre et al. ("*Ballevre*"). A copy of *Ballevre* is attached herewith as Exhibit D in the Evidence Appendix.

VII. ARGUMENT

A. LEGAL STANDARDS

1. Anticipation under 35 U.S.C. § 102(b)

Under 35 U.S.C. § 102(b) an invention is not patentable if it has been "patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application of patent in the United States." For example, an invention is not patentable if the claimed subject matter is "anticipated" by the prior art. Anticipation requires that a single prior art reference discloses each and every limitation of the claimed invention. *Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664 (Fed. Cir. 2003). The reference needs to "be enabling and describe the applicant's claimed invention sufficiently to have placed it in possession of a person of ordinary skill in the field of the invention." *ArthroCare Corp. v. Smith & Nephew Inc.*, 406 F.3d 1365, 1372, 74 USPQ2d 1749 (Fed. Cir. 2005) (quoting *In re Paulsen*, 30 F.3d 1475, 1479, 31 USPQ2d 1671 (Fed. Cir. 1994)).

2. Obviousness under 35 U.S.C. §103

The Federal Circuit has held that the legal determination of an obviousness rejection under 35 U.S.C. § 103 is:

> whether the claimed invention as a whole would have been obvious to a person of ordinary skill in the art at the time the invention was made…The foundational facts for the prima facie case of obviousness are: (1) the scope and content of the prior art; (2) the difference between the prior art and the claimed invention; and (3) the level of ordinary skill in the art…Moreover, objective indicia such as commercial success and long felt need are relevant to the determination of obviousness…Thus, each obviousness determination rests on its own facts.

In re Mayne, 41 U.S.P.Q. 2d 1451, 1453 (Fed. Cir. 1997).

In making this determination, the Patent Office has the initial burden of proving a *prima facie* case of obviousness. *In re Rijckaert*, 9 F.3d 1531, 1532, 28 U.S.P.Q. 2d 1955, 1956 (Fed. Cir. 1993). This burden may only be overcome "by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that

individual to combine the relevant teachings." *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q. 2d 1596, 1598 (Fed. Cir. 1988). "If the examination at the initial stage does not produce a prima facie case of unpatentability, then without more the applicant is entitled to grant of the patent." *In re Oetiker*, 24 U.S.P.Q. 2d 1443, 1444 (Fed. Cir. 1992).

Of course, references must be considered as a whole and those portions teaching against or away from the claimed invention must be considered. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve Inc.*, 796 F.2d 443 (Fed. Cir. 1986). "A prior art reference may be considered to teach away when a person of ordinary skill, upon reading the reference would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the Applicant." *Monarch Knitting Machinery Corp. v. Fukuhara Industrial Trading Co., Ltd.*, 139 F.3d 1009 (Fed. Cir. 1998), quoting, *In re Gurley*, 27 F.3d 551 (Fed. Cir. 1994).

B. THE CLAIMED INVENTION

Independent Claims 1-3 recite, in part, a method comprising the step of administering a nutritional composition including a protein source having at least 80% by weight of a component selected from the group consisting of whey protein and a protein mixture which simulates the amino acid profile of whey protein consisting of approximately 80% to about 90% by weight of casein. Appellants have surprisingly discovered that the administration of nutritional compositions that contain whey protein, or a protein mixture which simulates the amino acid profile of whey protein, as a protein source increases plasma glutamine levels in humans or animals. This is despite the fact that whey protein contains relatively low amounts of glutamine. Further, nutritional compositions that contain whey protein as a protein source provide glutamine levels much higher than those provided by nutritional compositions containing free amino acids including glutamine as protein source.

C. THE REJECTIONS OF CLAIMS 1-2 AND 6 UNDER 35 U.S.C. §102(b) SHOULD BE REVERSED BECAUSE *OPTIMUM NUTRITION* AS EVIDENCED BY *COSTELLO'S* IS NOT PROPER PRIOR ART

1. The product disclosed by *Optimum Nutrition* was not on sale or publicly disclosed before the priority date of the present application because the product disclosed in *Optimum Nutrition* is not the same product disclosed in *Costello's*

Appellants respectfully submit that the earlier version of *Optimum Nutrition* (e.g., the product featured in the publication by Costello's ("*Costello's*" attached as Exhibit E) and cited by the Examiner in the supplemental Office Action dated May 8, 2006) is not identical in formulation to the *Optimum Nutrition* being relied upon in the final Office Action dated October 16, 2006. For example, the whey protein product from *Optimum Nutrition* being relied upon in the final Office Action states that the formulation is "better than ever," which suggests that the formulation has been modified from an earlier version. Furthermore, the website for *Optimum Nutrition* currently discloses that the most recent formulation of the whey protein product is the third generation of *Optimum Nutrition* whey protein products. See, bodybuilding.com attached as Exhibit F.

If the whey protein product being relied upon in the final Office Action is, in fact, the second version of the *Optimum Nutrition* whey protein product, there is no definitive proof that this second version is the same formulation as the product featured in *Costello's* and that the exact product disclosed in *Optimum Nutrition* was on sale before the priority date of the present application. For example, the specific nutritional formulation of the catalogued whey protein nutrition product sold by *Costello's* is not disclosed or taught in any of the references cited by the Examiner. It remains possible that *Costello's* nutritional product referred to by the Examiner does not disclose or suggest a protein source having at least 80% by weight of a whey protein or a protein mixture which simulates the amino acid profile of whey protein as required, in part, by the present claims. Instead, *Costello's* nutritional product may also provide additional protein sources besides whey protein that amount to more than 20% of the total protein source.

In sum, Appellants respectfully submit that the *Optimum Nutrition* product formulation cited against the pending application is, in fact, not the same *Optimum Nutrition* product formulation sold by *Costello's* cited by the Examiner. Accordingly, Appellants respectfully

submit that the product disclosed by *Optimum Nutrition* was not on sale or publicly disclosed before the priority date of the present application (i.e. March 31, 1998) and therefore does not anticipate the present claims.

2. *Optimum Nutrition* as evidenced by *Costello's* fails to disclose or suggest every element of Claim 1

Appellants respectfully submit that *Optimum Nutrition* as evidenced by *Costello's* fails to disclose or suggest a method for increasing plasma glutamine concentration in a stressed mammal as required, in part, by Claim 1. In fact, *Optimum Nutrition* as evidenced by *Costello's* fails to disclose or suggest administering its compound to any stressed mammal, for example, to increase its plasma glutamine concentration in accordance with Claim 1.

D. THE REJECTIONS OF CLAIMS 1-20 UNDER 35 U.S.C. §103(a) SHOULD BE REVERSED BECAUSE THE EXAMINER HAS NOT ESTABLISHED A *PRIMA FACIE* CASE OF OBVIOUSNESS

1. One having ordinary skill in the art would not be motivated to combine the cited references to arrive at the present claims

Appellants respectfully submit that the Examiner has failed to consider the references as a whole and those portions teaching against or away the combination and from the claimed invention. Instead, the Examiner has improperly attempted to combine references that have different intended purposes and/or distinct modes of operation. As a result, Appellants submit that one having ordinary skill in the art would not be motivated to combine *Optimum Nutrition* as evidenced by *Costello's* and *Ballevre* to arrive at the present claims.

The whole premise of *Ballevre* is that carob protein is rich in glutamine and that its nutritional composition for improving plasma glutamine should include carob protein. *Ballevre* further teaches that its mixture of carob and whey proteins uses whey protein as the minor rather than the major component. See, *Ballevre*, column 4, lines 27-35; Example 2. For example, *Ballevre* discloses that carob protein comprises about 40% to about 100% by weight of the protein source of its nutritional composition, which results in the protein source in *Ballevre*

containing a minimum of "about 40%" of the protein source of carob. Because *Ballevre* teaches that it is essential to retain carob protein, it teaches away from a combination with *Optimum Nutrition* that is directed to a product comprising 100% whey proteins to assist in body building.

Moreover, if the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). This certainly applies here where one of the cited references is directed to a product that must comprise some and preferably a majority of carob protein (*Ballevre*) and the other cited reference is directed to a product comprising only whey protein (*Optimum Nutrition*) for body building. The specific formulation for each product as taught by the cited references is important and specific to that particular product. Because of these differences, one skilled in the art would not be motivated to modify or combine *Optimum Nutrition* and *Ballevre* to arrive at the present claims.

In sum, the cited references above are directed to completely different objectives and modes of operation. For at least the reasons discussed above, the combination of the cited references is improper.

2. Even if combinable, the cited references fail to disclose or suggest all of the elements of the claimed invention

Appellants respectfully submit that *Ballevre* and *Optimum Nutrition* as evidenced by *Costello's* fail to disclose or suggest every element of independent Claims 1 and 3. For example, *Ballevre* fails to disclose or suggest a method for increasing plasma glutamine concentration in a stressed mammal as required, in part, by Claim 1. *Ballevre* also fails to disclose or suggest a method for providing glutamine to a mammal suffering from injured, diseased or under-developed intestines as required, in part, by Claim 3.

As stated in Appellants' specification, the present invention is based on the surprising discovery that feeding whey protein to stressed or injured/diseased mammals, for example, in need of glutamine supplementation improves plasma glutamine status more than would be expected with regard to the lower amounts of glutamine present in whey protein. See, specification, page 3, lines 4-11. As is observed from Example 2 of Appellants' specification and known by one having ordinary skill in the art, whey protein contains a lower proportion of

glutamine than both casein and soy protein, yet better plasma and muscle glutamine status is obtained by feeding whey protein than by feeding casein and soy proteins. Thus, the present claims are directed to a novel way of increasing glutamine levels in stressed or injured/diseased mammals using whey protein or a protein mixture which simulates the amino acid profile of whey protein and not simply a way of supplementing with free glutamine.

In contrast to the present claims, *Ballevre* is directed to carob protein comprises about 40% to about 100% by weight of the protein source of its nutritional composition, which results in the protein source in *Ballevre* containing a minimum of "about 40%" of the protein source of carob. This means that the theoretical maximum whey or casein content would be about 60% (e.g. 100% - 40% = 60%) because carob protein comprises the majority of the protein source. This is a difference of 20% from what the present claims require and therefore does not reasonably fall within the "approximate" range. Moreover, the description of *Ballevre* in any event teaches away from this by teaching a maximum whey content (or mixture of whey and casein) of 30% of the protein source, which is even further from the claimed ranges. See, *Ballevre*, column 4, lines 28-36. As a result, Appellants respectfully submit that *Ballevre* fails to disclose or suggest the claimed methods of administering to a stressed or injured/diseased mammal a nutritional composition having the claimed ranges of whey protein OR a mixture which simulates the amino acid profile of whey protein.

Further, *Ballevre* is entirely directed to the use of a protein source comprising carob protein, which is rich in glutamine. As a result, it teaches away from Appellants' present claims wherein the protein source contains a low concentration of glutamine (e.g. because the protein source comprises at least 80% by weight whey protein). See, *Ballevre*, Abstract and column 2, lines 33-42. In fact, *Ballevre* is concerned with a glutamine rich nutritional composition used for glutamine supplemented diets. See, *Ballevre*, column 2, lines 27-30.

Optimum Nutrition as evidenced by *Costello's* also fails to disclose or suggest every element of the claimed invention. For example, *Optimum Nutrition* as evidenced by *Costello's* fails to disclose or suggest a method for increasing plasma glutamine concentration in a stressed mammal as required, in part, by Claim 1. *Optimum Nutrition* as evidenced by *Costello's* fails to disclose or suggest a method for providing glutamine to a mammal suffering from injured, diseased or under-developed intestines as required, in part, by Claim 3. In fact, *Optimum Nutrition* as evidenced by *Costello's* fails to disclose or suggest administering its compound to

any stressed or injured/diseased mammal, for example, to increase its plasma glutamine concentration in accordance with the present claims.

In sum, Appellants have discovered the novel way of increasing glutamine levels in mammals by providing nutritional compositions that have relatively low glutamine levels themselves. Appellants have carefully researched the desirability, applicability and levels of protein sources to be effectively used for such increases to occur. Nowhere does *Ballevre* or *Optimum Nutrition* recognize or successfully employ administering to a stressed or injured/diseased mammals the claimed nutritional products comprising a protein source having at least 80% by weight of a whey protein or a protein mixture which simulates the amino acid profile of whey protein to increase glutamine levels in the mammals. As a result, the cited references, alone or in combination, do not teach, suggest, or even disclose all of the elements of independent Claims 1 and 3 and the claims that depend from Claims 1 and 3, and thus, fail to render the claimed subject matter obvious.

For at least the reasons discussed above, the cited references are not properly combinable and/or fail to disclose or suggest every element of the present claims. Accordingly, Appellants respectfully submit that Claims 1-3 and Claims 4-16 that depend from Claims 1-3 are novel, nonobvious and distinguishable from the cited references and are in condition for allowance.

VIII. CONCLUSION

Appellants respectfully submit that the Examiner has failed to establish anticipation under 35 U.S.C. §102 and a *prima facie* case of obviousness under 35 U.S.C. §103 with respect to the rejections of Claims 1-16. Accordingly, Appellants respectfully submit that the anticipation and obviousness rejections are erroneous in law and in fact and should therefore be reversed by this Board.

A check in the amount of $500 is submitted herewith to cover the cost of the Appeal Brief. The Director is authorized to charge any additional fees which may be required, or to credit any overpayment to Deposit Account No. 02-1818. If such a withdrawal is made, please indicate the Attorney Docket No. 112701-036 on the account statement.

Respectfully submitted,

BELL, BOYD & LLOYD LLC

BY _____

Robert M. Barrett
Reg. No. 30,142
Customer No. 29157

Dated: May 14, 2007

CLAIMS APPENDIX

PENDING CLAIMS ON APPEAL OF U.S. PATENT APPLICATION SERIAL NO. 09/646,748

1. A method for increasing plasma glutamine concentration in a stressed mammal, the method comprising the step of administering to the stressed mammal a nutritional composition including a protein source having at least 80% by weight of a component selected from the group consisting of whey protein, and a protein mixture which simulates the amino acid profile of whey protein consisting of approximately 80% to about 90% by weight of casein, approximately 0.5% to about 2% by weight of isoleucine, about 2% to about 8% by weight of leucine, about 1% to about 5% by weight of cysteine, and about 1% to about 5% by weight of lysine.

2. A method for increasing muscle glutamine concentrations in a mammal, the method comprising the step of administering to the mammal a nutritional composition including a protein source having at least 80% by weight of a component selected from the group consisting of whey protein, and a protein mixture which simulates the amino acid profile of whey protein consisting of approximately 80% to about 90% by weight of casein, approximately 0.5% to about 2% by weight of isoleucine, about 2% to about 8% by weight of leucine, about 1% to about 5% by weight of cysteine, and about 1% to about 5% by weight of lysine.

3. A method for providing glutamine to a mammal suffering from injured, diseased or under-developed intestines, the method comprising the step of administering to the mammal a nutritional composition including a protein source having at least 80% by weight of a component selected from the group consisting of whey protein, and protein mixture which simulates the amino acid profile of whey protein consisting of approximately 80% to about 90% by weight of casein, approximately 0.5% to about 2% by weight of isoleucine, about 2% to about 8% by weight of leucine, about 1% to about 5% by weight of cysteine, and about 1% to about 5% by weight of lysine.

4. The method of Claim 3 wherein the mammal is a pre-term infant having an under-developed intestine.

5. The method of Claim 4 wherein the whey protein is hydrolyzed and the protein source further comprises arginine, tyrosine and histidine.

6. The method of Claim 1 wherein the whey protein is hydrolyzed whey protein.

7. The method of Claim 6 wherein the hydrolyzed whey protein contains less than about 5% by weight of free amino acids, about 15% to about 55% by weight of peptides having a molecular weight of less than 1000 Da, about 20% to about 55% by weight of peptides having a molecular weight of 1000 Da to 5000 Da, and about 15% to about 35% by weight of peptides having a molecular weight of greater than 5000 Da.

8. The method of Claim 1 wherein the protein source provides about 10% to about 20% of the energy of the nutritional composition.

9. The method of Claim 1 wherein the nutritional composition further includes a lipid source which provides about 20% to about 50% of the energy of the nutritional composition, the lipid source comprising a mixture of medium chain and long chain fatty acids.

10. The method of Claim 1 wherein the nutritional composition further includes a carbohydrate source which provides about 35% to about 65% of the energy of the nutritional composition.

11. The method of Claim 2 wherein the protein source provides about 10% to about 20% of the energy of the nutritional composition.

12. The method of Claim 2 wherein the nutritional composition further includes a lipid source which provides about 20% to about 50% of the energy of the nutritional composition, the lipid source comprising a mixture of medium chain and long chain fatty acids.

13. The method of Claim 2 wherein the nutritional composition further includes a carbohydrate source which provides about 35% to about 65% of the energy of the nutritional composition.

14. The method of Claim 3 wherein the protein source provides about 10% to about 20% of the energy of the nutritional composition.

15. The method of Claim 3 wherein the nutritional composition further includes a lipid source which provides about 20% to about 50% of the energy of the nutritional composition, the lipid source comprising a mixture of medium chain and long chain fatty acids.

16. The method of Claim 3 wherein the nutritional composition further includes a carbohydrate source which provides about 35% to about 65% of the energy of the nutritional composition.

EVIDENCE APPENDIX

EXHIBIT A: Final Office Action dated October 16, 2006

EXHIBIT B: Advisory Action dated February 6, 2007

EXHIBIT C: 100% Whey Proteins 5 lbs by Optimum Nutrition ("*Optimum Nutrition*"), cited by the Examiner in the Office Action dated October 16, 2006

EXHIBIT D: U.S. Patent No. 5,849,335 to Ballevre et al. ("*Ballevre*"), cited by the Examiner in the Office Action dated October 16, 2006

EXHIBIT E: The publication by Costello's ("*Costello's*"), cited by the Examiner in the supplemental Office Action dated May 8, 2006)

EXHIBIT F: Web page of www.bodybuilding.com/store/opt/print.php taken on January 2, 2007

RELATED PROCEEDINGS APPENDIX

None

EXHIBIT A

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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Alexandria, Virginia 22313-1450
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/646,748	12/11/2000	Julio Boza	112701 036	7778

7590 10/16/2006

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EXAMINER	
MOHAMED, ABDEL A	
ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 10/16/2006

Due: 1-16-07

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)	
09/646,748	BOZA, JULIO	
Examiner	**Art Unit**	
Abdel A. Mohamed	1654	

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT TO REMARKS AND STATUS OF THE CLAIMS

1. The remarks filed 08/03/06 is acknowledged, entered and considered. Claims 1-16 are now pending in the application. The rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) over the prior art of record are maintained for the reasons set forth in the previous Office action.

ARGUMENTS ARE NOT PERSUASIVE

CLAIMS REJECTION-35 U.S.C. § 102(b)

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2 and 6 remain rejected under 35 U.S.C. 102(b) as being anticipated by the product 100% Whey Protein 5 lbs, which is available in the market by Optimum Nutrition.

Applicant's arguments filed 08/03/06 have been fully considered but they are not persuasive. Applicant has argued that the Patent Office has failed to demonstrate that *Optimum Nutrition* was on sale before the priority date of the present application (i.e., March 31, 1998). Moreover, the Patent Office has failed to show that any earlier version of the product of *Optimum Nutrition* was identical to that now sold. Accordingly, the rejection of claims 1-2 and 6 under 35 U.S.C. § 102(b) be withdrawn is

unpersuasive. Contrary to Applicant's arguments, the Examiner has provided a supplemental Office action mailed 05/08/06 as Paper No. 20060504 to clarify the date of public sale for the product 100% Whey Protein applied in 102(b) and 103(a) rejections of the Office action mailed 05/05/06 as Paper No. 20060427. The Costello's Catalog cited on PTO-892 and provided to Applicant in which *Optimum Nutrition* put their 100% whey product on sale (i.e., in the market) in Fall 1997 as evidenced in the provided Costello's Catalog that lists 100% Whey Protein Product (code 02-288 and 02-289, available in the 2# size in chocolate and vanilla flavors). Thus, the Patent Office has clearly demonstrated that *Optimum Nutrition* was on sale before the priority date of the present application (i.e., 03/31/98), and as such, the rejection under 35 U.S.C. § 102(b) for claims 1, 2 and 6 is maintained for the reasons of record.

CLAIMS REJECTION-35 U.S.C. § 103(a)

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over the product 100% Whey Protein 5 lbs, which is available in the market by Optimum Nutrition taken with Ballevre et al (U.S. Patent No. 5,849,335.

Applicant has argued that one of ordinary skill in the art would not be motivated to combine *Optimum Nutrition* and Ballevre to arrive at the present claims. Ballevre discloses that carob protein comprises about 40% to about 100% by weight of the protein source of its nutritional composition, which results in the protein source in Ballevre containing a minimum of "about 40%" of the protein source of carob. Because Ballevre teaches that it is essential to retain carob protein, it teaches away from a combination with *Optimum Nutrition* that is directed to a product comprising 100% whey proteins. If the proposed modification would render the prior art invention being modified unsatisfactory for its intended purposes, then there is no suggestion or motivation to make the proposed modification is unpersuasive.

Contrary to Applicant's arguments, the claims of the instantly claimed invention are broad because claims 1-16 are directed to methods for increasing glutamine by using whey protein or a protein mixture administered to a patient to increase plasma glutamine concentration in stressed mammal (claim 1), to increase muscle glutamine concentration in mammal (claim 2), to use as nutritional/therapeutic composition to a mammal suffering from injured, diseased or under-developed intestines (claim 3), wherein the mammal is a pre-term infant having an under-developed intestines (claim 4), wherein the protein is hydrolyzed (claims 5 and 6) and having the various molecular weights recited in claim 7, wherein the protein source provide energy of the nutritional

composition thereof (claims 8, 11 and 14), wherein the nutritional composition further includes a lipid source (claims 9, 12 and 15) and wherein the nutritional composition includes carbohydrate source (claims 10, 13 and 16).

The Examiner acknowledges that the primary reference of *Optimum Nutrition* teaches the use of a nutritional composition comprising 100% whey protein for dietary supplement, however, the secondary reference of Ballevre et al ('335 patent) teaches a nutritional composition comprising a protein source including whey protein and a protein mixture having the amino acid profile of whey protein which is administered to stressed patients to increase the plasma glutamine concentration, or administered as nutritional support for increasing muscle glutamine concentration in athletes after exercise, or administered to patients suffering from injured or diseased intestines or to maintain the physiological functions of the intestines particularly in under-developed intestines (e.g., a pre-term infant or babies) as disclosed on the abstract; col. 1, lines 44-50; col. 3, lines 1-25; col. 6, lines 13-38; claims 24, 26-28 and 30. Thus, clearly meeting the limitations of claims 1-4.

On col. 4, the '335 patent discloses the use of nutritional composition wherein the whey protein is hydrolyzed whey protein, the protein source provides about 10% to about 30% of the energy of the nutritional composition, the nutritional composition further includes a lipid source which provides about 20% to about 40% of the energy of the nutritional composition and the lipid source comprises a mixture of medium chain and long chain fatty acids, and as such meet the limitations of claims 5, 6, 8, 9, 11, 12, 14 and 15. The secondary reference also discloses a nutritional composition which

further includes a carbohydrate source which provide about 35% to about 60% of the energy of the nutritional composition and as such meet the limitations of claim 10, 13 and 16 (See e.g., col. 2, lines 46-64; col. 4, lines 4-56 and Examples 2-4).

Therefore, given the teachings of the product of primary reference of Optimum Nutrition which teaches the use of nutritional composition of 100% whey protein for dietary supplement, one of ordinary skill in the art would have been motivated at the time the invention was made to adapt the above scheme of the administration of nutritional composition, which contains whey protein (or a protein mixture which stimulates its acid profile) as a protein source for the same purposes (i.e., for increasing glutamine levels in plasma or muscle of a stressed patient, pre-term baby or athletes) of the secondary reference of '335 patent. Further, such features are known or suggested in the art, as seen in the secondary reference, and including such features into the composition/formulation of the primary reference would have been obvious to one of ordinary skill in the art to obtain the known and recognized functions and advantages thereof.

Therefore, the combined teachings of the cited references makes obvious the claimed invention because at the time the invention was made based on the combined teachings of the cited references and for the reasons given above, one of ordinary skill in the art would have easily adapt of using the already known process of the whey protein hydrolysate comprising glutamine for nutritional purposes (i.e., a metabolic process), which is a mechanism wherein the sum total of chemical and physical processes within the body related to release of energy by the breakdown of chemical

fuel and the use of that energy by the cells for their own work. Thus, the combined teachings of the cited references clearly showing the known principles of physiology that naturally occurs after intake of food or meal that increases plasma glutamine concentration in mammals, increases muscle glutamine concentration in mammal and provides treatment to patients suffering from injured, diseased or under-developed intestines.

Accordingly, claims 1-16 are *prima facie* obvious over the combined teachings of the cited references, because it is an obvious modification of the cited references combined teachings for a nutritional composition including a protein source having at least 80% by weight of a component selected from either whey protein or a mixture which stimulates the amino acid profile of whey protein consisting of approximately 80% to about 90% by weight for nutritional purposes in the manner claimed. Thus, it is made obvious by the combined teachings of the prior art since the instantly claimed invention which falls within the scope of the prior art teachings would have been obvious because as held in host of cases including *Ex parte Harris*, 748 O.G. 586; *In re Rosselete*, 146 USPQ 183; *In re Burgess*, 149 USPQ 355 and as exemplified by *In re Betz*, "the test of obviousness is not express suggestion of the claimed invention in any and all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them".

ACTION IS FINAL

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CONCLUSION AND FUTURE CORRESPONDANCE

5. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272 0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tsang Cecilia can be reached on (571) 272 0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JON WEBER
SUPERVISORY PATENT EXAMINER

AAM Mohamed/AAM
October 6, 2006

EXHIBIT B

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/646,748	12/11/2000	Julio Boza	112701 036	7778

7590 02/06/2007

Robert M Barrett
P O Box 1135
Chicago, IL 60690-1135

EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
02/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/646,748	**Applicant(s)** BOZA, JULIO
	Examiner Abdel A. Mohamed	**Art Unit** 1654

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 03 January 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: 1-16.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☒ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
    See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Continuation of 11. does NOT place the application in condition for allowance because: Applicant's arguments that the whey protein product is the third generation of Optimum Nutrition whey protein products as evidenced by Exhibit A, and as such, the Patent Office has failed to demonstrate that this version is the same formulation as the product featured in Costello's and the Optimum Nutrition was on sale before the priority date of the present application is unpersuasive. Contrary to Applicant's arguments, the Optimum Nutrition is proper prior art because Applicant has not demonstrated that there is difference between the claimed hydrolyzed whey protein and the Costello's Health Distributor's 1977 product catalog along with a copy of the specific page of the catalog that lists 100% whey protein product (Codes 02 288 and 02 289, available in 2 # size in chocolate and vanilla flavors). Thus, clearly demonstrating that Optimum Nutrition was on sale before the priority date of the present application, and as such the rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) over the prior art of record are maintained for the reasons set forth in the previous Office action .

Jon Weber
Supervisory Patent Examiner

EXHIBIT C

100% Whey Protein 5 lbs by Optimum Nutrition

5 lbs; 77-80 servings

List Price: $43.99
Our Price: $29.95

You Save $14.04!

Product Code: 100WHEYPROTEIN5LBS

*Choose your options then press "Add to Cart"

Email a Friend

Flavor*: Strawberry (7406)

Qty: 1 ADD TO CART Add to Wish List

*Enter keyword or item #

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J K L M N O P Q R
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Protein Powder
Vitamins & Minerals
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Weight Gainers

Herbs
Antioxidants
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Bodybuilding Videos
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Description **Related Articles**

Millions and Millions of satisfied customers can't be wrong!

- Superior Blend of Whey Protein Isolates, Concentrates, and Hydrolysates
- Gold Standard has Whey Protein Isolates as the primary protein source.
- Only 3 grams of Carbohydrates
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Since the very beginning, ON's 100% Whey Protein has raised the standard by which all whey protein supplements are judged. Now years later, we're raising the bar again.

Like it's predecessors, ON's 100% Whey Protein contains Optimum Nutrition's exclusive, proprietary blend of...

1. Microfiltered Whey Protein Isolates
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to give you more of what you want (pure, unadulterated whey protein) with less of what you don't (fat, saturated fat, cholesterol, lactose, and other carbohydrates) with every serving. In fact, ON's

You may also like:

Optimum Glutamine Powder 1000 g
Our Price: $45.35

Optimum Creatine Powder 2000 g
Our Price: $47.63

Related Products

100% Any Whey
Our Price: $24.99

Perfect Low Carb Isopure

EXHIBIT D

US005849335A

United States Patent [19]

Ballèvre et al.

[11] Patent Number: 5,849,335

[45] Date of Patent: Dec. 15, 1998

[54] **COMPOSITION AND METHOD FOR PROVIDING GLUTAMINE**

[75] Inventors: **Olivier Ballèvre**, Lausanne, Switzerland; **Krishna Anantharaman**, Bridgewater, Conn.; **Julio Boza**, La Conversion-Lutry; **Clara-Lucia Garcia-Rodenas**, Mollie-Margot, both of Switzerland

[73] Assignee: **Nestec S.A.**, Vevey, Switzerland

[21] Appl. No.: **869,866**

[22] Filed: **Jun. 2, 1997**

[51] **Int. Cl.**[6] **A61K 35/20**; A61K 35/78; A61K 39/385

[52] **U.S. Cl.** **424/535**; 424/195.1; 514/562; 514/563

[58] **Field of Search** 514/563, 562; 424/195.1, 535

[56] **References Cited**

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Primary Examiner—Leonard Schenkman
Attorney, Agent, or Firm—Hill & Simpson

[57] **ABSTRACT**

A nutritional composition for providing glutamine to a human or animal. The protein source of the composition includes carob protein which is rich in glutamine. A source of Met may also be included. The composition may be used in the treatment of stressed patients; for example those patients who are critically ill, suffering from sepsis, injury, burns, or inflammation, or who are recovering from surgery. Further, the composition may be used to raise plasma glutamine levels; for example in athletes after intense exercise.

33 Claims, No Drawings

COMPOSITION AND METHOD FOR PROVIDING GLUTAMINE

FIELD OF THE INVENTION

This invention relates to a nutritional composition for providing glutamine to a human or animal. The invention also relates to a method for providing glutamine to a human or animal and to a method for the treatment of humans and animals requiring supplemental glutamine.

BACKGROUND OF THE INVENTION

The amino acid glutamine has many important functions in the body. For example, glutamine acts as the primary vehicle for transfer of amino nitrogen from skeletal muscle to visceral organs, as a fuel for the rapidly dividing cells of the gastrointestinal tract and immune system, and as a substrate that permits the kidneys to excrete acid loads and protect the body against acidosis. Further, there is increasing evidence that glutamine is essential to the proper functioning of host defense mechanisms and wound healing.

Despite these functions, glutamine is traditionally classified as non-essential amino acid. The reason is that the body is generally able to synthesize sufficient glutamine for its needs from glutamate and glutamic acid. Also, glutamine is the most abundant amino acid in the blood and free amino acid pool of the body. However, this is only true in periods of good health and does not apply to preterm babies. During periods of illness, the metabolic rate of glutamine increases and the body is not able to synthesize sufficient glutamine to meet its needs. This is particularly true during episodes of stress such as sepsis, injury, burns, inflammation, diarrhea and surgery. During episodes of stress, there is a marked increase in glutamine consumption by the gastrointestinal tract, immune cells, inflammatory tissue and the kidney. This consumption may far outstrip the endogenous rate of synthesis of glutamine. As the deficiency becomes manifest, tissue function alters, morphological changes may be observed, and a negative nitrogen balance arises. Similarly, preterm babies have a lower rate of glutamine synthesis; often insufficient for needs. Further, it is found that athletes, after intense exercise, have reduced levels of glutamine in their plasma.

The administration of glutamine supplemented diets to preterm babies, during periods of stress, or to athletes has resulted in improvement of the person's condition. For example, glutamine supplemented diets have been shown to regenerate muco-proteins and intestinal epithelium, support gut barrier function, shorten hospital stay, improve immune function, and enhance patient survival (Stehle et al; 1989; *Lancet,* 1:231–3; Hammerqvist et al; 1989; *Ann. Surg.;* 209:455–461; Li et al; 1995; *J. Parenter. Enteral Nutr.,* 18, 303–307 and Gianotti et al; 1995; *J Parenter. Enteral Nutr.,* 19, 69–74). Therefore glutamine is now considered to be a conditionally essential amino acid for critically ill and other stressed patients (Lacey et al; 1990; *Nutrition Review,* 48:297–309).

The additional need for glutamine during periods of stress must come from an exogenous source such as diet. However the supplementation of nutritional formulas with glutamine has traditionally not been performed because glutamine has long been considered to be a non-essential amino acid. Also glutamine is only slightly soluble in water and, more importantly, is relatively unstable in solution. To overcome the stability problem, it has been proposed to supplement powdered formulas with L-glutamine. These formulas are then reconstituted immediately prior to administration.

However, for enteral formulas, this approach has not proved to be particularly successful since glutamine in its free form may be converted to glutamate by stomach acids prior to absorption. Also, health care professionals prefer ready-to-consume liquid formulas as opposed to powdered formulas.

Another method of supplementing diet with glutamine has centered on the use of gluten or gluten hydrolysates as a protein source for nutritional compositions. Gluten is particularly rich in glutamine and is hence a good source of glutamine. Also, the use of gluten or a gluten hydrolysate offers the advantage of providing the glutamine in a form which is stable and relatively soluble. However gluten is potentially allergenic and this has severely limited its use in nutritional formulas. This problem may be ameliorated to some extent by using a gluten hydrolysate instead of gluten and a nutritional composition based on gluten hydrolysate is commercially available under the trade name Nutricomp® Immun. However, although the risk from allergenic reaction is much reduced, it has not been removed entirely.

A yet further approach has been to supplement nutritional formulas with synthetic dipeptides such as L-alanyl-L-glutamine or L-glycyl-L-glutamine. These dipeptides are stable in solution and have been shown to be an effective form of glutamine supplementation. However, synthetic peptides of this nature may significantly increase the cost of the nutritional formulas.

Therefore there is a need for a nutritional composition which is rich in an inexpensive, stable form of glutamine and which has a negligible risk of inducing allergenic reactions.

SUMMARY OF THE INVENTION

Accordingly, in one aspect, this invention provides a nutritional composition for providing glutamine, the composition being in powdered, liquid concentrate or ready-to-drink liquid form and comprising: a protein source including carob protein.

It has been surprisingly discovered that carob protein provides an excellent source of glutamine in a form which is stable and which has very little or no risk of inducing allergenic reactions. Further, carob protein provides the additional advantage of a substantially balance amino acid profile . Also, carob protein is rich in arginine; an amino acid which is useful in the nutrition of stressed patients suffering impairment of the immune system.

In another aspect, this invention provides a nutritional composition for providing glutamine, the composition having a protein source comprising carob protein and a source of Met. Preferably a source of Cys and Met is provided to provide at least 24 mg/g protein of Cys and Met. Preferably the source of Cys and Met is selected from whey or casein or both. A source of tryptophan may also be included.

In a yet further aspect, this invention provides a nutritional composition for providing glutamine, the composition having a protein source comprising an isolate or hydrolysate of carob protein.

Preferably, the nutritional composition further comprises a carbohydrate source; and a lipid source. The protein source preferably provides about 10% to about 30% of the energy of the nutritional composition; the carbohydrate source about 35% to about 60% of the energy of the nutritional composition; and the lipid source about 20% to about 40% of the energy of the nutritional composition.

In another aspect, this invention provides a method of providing glutamine to a human or animal, the method comprising enterally administering to the human or animal

an effective amount of a nutritional composition having a protein source including carob protein.

In yet another aspect, this invention provides a method of increasing plasma glutamine levels in a human or animal, the method comprising enterally administering to the human or animal an effective amount of a nutritional composition having a protein source including carob protein.

Preferably the human or animal is a stressed patient, preterm baby, or athlete. Examples of stressed patients are patients who are critically ill, or who are suffering from sepsis, injury, burns, or inflammation, or patients recovering from surgery.

In a further aspect, this invention provides a method of improving the immune function of a stressed patient or athlete by providing glutamine and arginine to the patient, the method comprising administering to the patient or athlete an effective amount of a nutritional composition having a protein source including carob protein.

In a further aspect, this invention provides a method of providing glutamine to patients suffering from injured or diseased intestines or to maintain the physiological functions of the intestine, the method comprising enterally administering to the patient an effective amount of a nutritional composition having a protein source including carob protein.

In a yet further aspect, this invention provides the use of carob protein in the preparation of an enterally administrable, nutritional composition for providing glutamine to a human or animal.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS OF THE INVENTION

Embodiments of the invention are now described by way of example only. The invention is concerned with the provision of glutamine to humans or animals and is based on the use of carob protein as a source of glutamine. Carob protein, usually in the form of carob germ protein, may be obtained from carob germ meal, a by-product obtained from the germ of the carob bean (*Ceratonia siliqua*) after the separation of the gums and fibrous coating of the seed. Carob germ meal contains about 40% to about 60% protein and is hence an excellent source of protein. Further, the carob bean is a perennial tree which is widely cultivated; particularly in the Mediterranean region and is hence readily available.

Many attempts at determining the amino acid composition of carob protein have been made in the past. All reported attempts have used techniques based upon acid hydrolysis of the protein followed by automated amino acid analysis. Although these techniques provide reasonably accurate results for most amino acids, they provide poor results for glutamine. The reason is that glutamine breaks down in the presence of heat and acid to form glutamic acid and ammonia. Consequently almost all of the reported analyses of carob protein report glutamine and glutamic acid as a summation value; if reported at all. However procedures have recently been developed which permit the accurate determination of protein and peptide bound glutamine. For example, methods involving the conversion of glutamine residues to acid stable L-2,4-diaminobutyric acid in the presence of bis(1,-trifluoroacetoxy)iodobenzene (Kuhn et al; 1996; *J Parent. Enteral Nutr,* 20, 4:292–295) or methods involving the enzymatic hydrolysis of the protein. When analyzed using these techniques, carob protein has a glutamine content of about 15.5 to about 17.5 g/100 g amino acids. In other words, relatively rich in glutaminc and an excellent source of glutamine. Further carob protein has the advantage that it contains about 12 g/100 g amino acids of arginine.

The carob protein may be in any suitable form, for example in the form of carob germ meal, a carob germ protein isolate or concentrate, or a carob germ protein hydrolysate. Preferably, the carob protein is treated to inactivate any proteolytic inhibitors which may be present. This may be carried out, for example, by subjecting the carob protein to heat treatment.

The protein source may include other types of protein in addition to carob protein; for example, casein, whey, soy, rice and oat bran protein, or mixtures thereof. The protein may be in intact form or hydrolyzed form. Further, the protein source may include free amino acids. Although carob protein has a reasonably well balanced amino acid profile which fulfills the recommendations of the FAO/WHO expert committee for the essential amino acid requirements for children>2 years, the amino acid profile may be further improved by mixing in other types of protein or free amino acids. This is particularly the case with other types of protein or free amino acid mixtures which are rich in sulfur-containing amino acids such as methionine and cysteine. Whey and casein are particularly suitable source of Met and Cys. A source of tryptophan is also conveniently included; for example in free amino acid form.

The carob protein may provide about 40% to about 100% by weight of the protein source; for example about 60% to about 80% by weight. The protein source preferably includes whey, casein, or mixtures of whey and casein; for example in an amount of about 10% to about 30% by weight. The protein source preferably provides about 10% to about 30% of the energy of the nutritional composition; for example about 15% to about 25% of the energy of the nutritional composition.

The carbohydrate source may provide about 35% to about 60% of the energy of the composition. For example, the carbohydrate source may provide about 45% of the energy of the nutritional composition. Several carbohydrates may be used including maltodextrin, corn starch, or sucrose, or mixtures thereof. Preferably the carbohydrate source is free from lactose.

The lipid source may provide about 20% to about 40% of the energy of the composition. For example, the lipid source may provide about 30% of the energy of the nutritional composition. The lipid source may include a mixture of medium chain triglycerides (MCT) and long chain triglycerides (LCT). For example, the lipid source may include at about 20% to about 80% by weight of medium chain triglycerides. For example, medium chain triglycerides may make up about 70% by weight of the lipid source. Suitable sources of long chain triglycerides are canola oil, soy oil, milk fat, corn oil, residual milk fat, and soy lecithin, or mixtures thereof. Coconut oil is a suitable source of medium chain triglycerides.

The lipid source may have a lipid profile designed to have a polyunsaturated fatty acid omega-6 (n-6) to omega-3 (n-3) ratio of about 4:1 to about 15:1. For example, the n-6 to n-3 fatty acid ratio may be about 7:1. Further, for patients suffering from inflammatory conditions, the lipid source may contain low levels of omega-6 fatty acids and higher levels of omega-3 fatty acids. Preferably the omega-6 fatty acids provide less than about 10% of total energy. For example these polyunsaturated fatty acids may provide about 4% of total energy. Decreasing the levels of these polyunsaturated fatty acids is believed to decrease sensitiv-

ity to peroxydation; which may be beneficial in the treatment of inflammatory diseases. In addition to the absorption/tolerance benefits of a moderate content of long chain triglycerides, the nutritional composition is less likely to be immunosuppressive due to the low content of omega-6 fatty acids.

The enteral composition preferably includes a complete vitamin and mineral profile. For example, sufficient vitamins and minerals may be provided to supply about 75% to about 250% of the recommended daily allowance of the vitamins and minerals per 1000 calories of the nutritional composition.

The nutritional composition may include a source of beta-carotene. Beta-carotene, formerly considered only as a precursor to vitamin A, is an important nutrient with antioxidant properties. For example, the composition may include about 0.5 to about 2.0 mg of beta-carotene per 1000 calories. This amount of beta-carotene is sufficient to maintain plasma beta-carotene concentration in the patient.

The nutritional composition may be in any suitable form. For example, the composition may be in the form of formulas such as soluble powders, liquid concentrates, or ready-to-use formulations. Ready to use formulations are particularly preferred. The composition may be fed to a patient via a nasogastric tube or by having the patient drink it. Various flavors, fibers and other additives may also be present. The composition may also be in the form of common foodstuffs; for example yogurts, soups, pastas, porridges, breakfast cereals, convenience foods such as muesli bars, and the like. For animals such as pets, the composition may be in the form of dried or canned petfood.

The nutritional composition may be produced as is conventional; for example, for formulas, the nutritional composition may be prepared by blending together the protein source, the carbohydrate source, and the lipid source. If used, the emulsifiers may be included in the blend. The vitamins and minerals may be added at this point but are usually added later to avoid thermal degradation. Any lipophilic vitamins, emulsifiers and the like may be dissolved into the lipid source prior to blending. Water, preferably water which has been subjected to reverse osmosis, may then be mixed in to form a liquid mixture. The temperature of the water is conveniently about 50° C. to about 80° C. to aid dispersal of the ingredients. Commercially available liquefiers may be used to form the liquid mixture.

The liquid mixture may then be thermally treated to reduce bacterial loads. For example, the liquid mixture may be rapidly heated to a temperature in the range of about 80° C. to about 110° C. for about 5 seconds to about 5 minutes. This may be carried out by steam injection or by heat exchanger; for example a plate heat exchanger.

The liquid mixture may then be cooled to about 60° C. to about 85° C.; for example by flash cooling. The liquid mixture is then homogenized; for example in two stages at about 7 MPa to about 40 MPa in the first stage and about 2 MPa to about 14 MPa in the second stage. The homogenized mixture may then be further cooled to add any heat sensitive components; such as vitamins and minerals. The pH and solids content of the homogenized mixture is conveniently standardized at this point.

If it is desired to produce a powdered nutritional composition, the homogenized mixture is transferred to a suitable drying apparatus such as a spray drier or freeze drier and converted to powder. The powder should have a moisture content of less than about 5% by weight. If it is desired to produce a liquid nutritional composition, the homogenized mixture is preferably aseptically filled into suitable containers. Aseptic filling of the containers may be carried out by pre-heating the homogenized mixture (for example to about 75° to 85° C.) and then injecting steam into the homogenized mixture to raise the temperature to about 140° to 160° C.; for example at about 150° C. The homogenized mixture may then be cooled, for example by flash cooling, to a temperature of about 75° to 85° C. The homogenized mixture may then be homogenized, further cooled to about room temperature and filled into containers. Suitable apparatus for carrying out aseptic filling of this nature is commercially available.

The nutritional composition may be used as a nutritional support. In particular, the nutritional composition may be used to provide nutrition and glutamine to animal and humans. In particular, the nutrition composition may be used to provide nutrition and glutamine to stressed patients; for example for patients who are critically ill, or who are suffering from sepsis, injury, burns, or inflammation, or patients recovering from surgery. Further, the nutritional composition may be used to provide glutamine to patients suffering from injured or diseased intestines or to maintain the physiological functions of the intestine. Moreover, the nutritional composition may be used to raise plasma glutamine levels in humans and animals.

Further, since the nutritional composition contains enriched levels of arginine, the nutritional composition may also be used as a source of both glutamine and arginine; for example for patients suffering immune system impairment.

The nutritional composition may also be used to provide glutamine to athletes after intense exercise or to preterm babies.

It is to be understood that, although the nutritional composition is intended primarily for patients who require supplemental glutamine, it may also be used as a source of nutrition for people who are not suffering from any illness or condition.

The nutritional composition may form the sole source of nutrition or form a supplement to other nutritional sources; including parenterally administered nutrition.

The amount of the nutritional composition required to be fed to a patient will vary depending upon factors such as the patient's condition, the patient's body weight, the age of the patient, and whether the nutritional composition is the sole source of nutrition. However the required amount may be readily set by a medical practitioner. In general, sufficient of the nutritional composition is administered to provide the patient with about 1 g protein to about 4.0 g protein per kg of body weight per day. For example, an adult, critically ill patient may be administered about 1.5 g protein to about 2.0 g protein per kg of body weight per day, a preterm infant may be administered about 2.0 g protein to about 4.0 g protein per kg of body weight per day, and a infant may be administered about 2.0 g protein to about 3.0 g protein per kg of body weight per day. Further, for stressed patients, sufficient of the nutritional composition is preferably administered to provide the patient with about 10 g to about 25 g of glutamine per day. The nutritional composition may be taken in multiple doses, for example 2 to 5 times, to make up the required daily amount or may taken in a single dose.

Example 1

Young, weaned male rats, which are 21 days old are used. The rats are weighed and then fed for three days on a diet which contains carbohydrates, lipids and n10% casein protein and which is supplemented with 0.2% by weight

methionine. The rats have free access to the diet and water. The rats are then weighed again. Two experimental diets are prepared by subjecting carob meal to heat treatment at 121° C. for about 30 minutes to inactivate proteolytic inhibitors. Methionine is then added to a level of 0.2% by weight. The mixture is then formulated with carbohydrates and lipids to provide two feeds; one containing about 10% by weight of carob protein (Feed 1) and the other containing about 20% by weight carob protein (Feed 2).

A group of rats is divided into three different sub-groups. One sub-group is provided with the casein based diet as control, another sub-group is provided Feed 1 and the third sub-group is provided Feed 2. All rats have free access to water and the feeds for the duration of the study. The rats are each weighed prior to commencement of the study and after the study. The study is continued for 4 weeks.

The rats fed Feed 1 and Feed 2 grow and gain weight at substantially the same rate as those fed the control diet. Further, the protein efficiency ratio (PER) for Feeds 1 and 2 is determined to be about 2.95; which is acceptable. The rats fed Feeds 1 and 2 are examined for toxic effects and none are found.

The trial indicates that feeds containing carob protein are well tolerated, support growth and have an acceptable PER.

Example 2

A ready-to-drink nutritional composition is prepared. The nutritional composition includes the following components:

Component	Amount per liter	Energy %
Protein		25
Carob germ: acid whey (80:20)		
Carbohydrate		45
Corn syrup solids		
Sucrose		
Lipids		30
Corn oil, Canola oil, Soy lecithin, Residual Milk fat, Coconut oil (MCT's)		
Vitamins		
Vitamin A	4000 IU	
β-carotene	2.0 mg	
Vitamin D	400 IU	
Vitamin E	60 IU	
Thiamin	3.0 mg	
Pyridoxine	4.0 mg	
Biotin	400 μg	
Minerals		
Zinc	24 mg	
Copper	2.0 mg	
Magnesium	4.0 mg	
Selenium	100 μg	
Sodium	876 mg	
Potassium	1500 mg	
Chloride	1300 mg	

The nutritional composition has an energy density of 1500 kcal/l and a ratio of ω6 fatty acids to ω3 fatty acid of about 7:1. The nutritional composition has the following amino acid composition:

Amino acid	Amount (mg/g protein)	Percentage of FAO/WHO requirements for > 2 years
Ile	37.94	135%
Leu	76.1	115%
Lys	68.1	117%
Met	11.4	—
Cys	17.9	—
Met + Cys	29.3	117%
Phe	32.9	—
Tyr	33.6	—
Phe + Tyr	66.5	106%
Thr	40.8	120%
Trp	11.0	100%
Val	42.8	122%
Arg	102.4	—
His	25.9	136%
Ala	44.0	—
Asp	89.3	—
Glu + Gln	243.4	—
Gln	149.2	—
Gly	42.9	—
Pro	38.4	—
Ser	45.3	—

Therefore the nutritional composition fully meets the FAO/WHO recommendations for children over the age of 2 years. Further, the nutritional composition contains about 15 g/100 g of amino acids of glutamine and about 10 g/100 g of amino acids of arginine.

Example 3

Twelve adults, of both sexes and between the ages of 20 to 60 years, are recruited for the study. All adults have been diagnosed as requiring oesogastrectomy surgery. The patients are separated into two groups, a control group and a test group.

One day prior to undergoing surgery, the glutamine concentrations in intracellular skeletal muscle and plasma are determined for each patient. Further determinations of glutamine concentrations in intracellular skeletal muscle and plasma are made on days 1, 2, 4, 8, and 12 after surgery. The weight of the patient one day prior to undergoing surgery and 12 days after surgery are determined. Each patient's wound is examined on days 4 and 12 after surgery.

After undergoing surgery, all patients are fed for two days using a standard parenteral formula. The parenteral formula contains less than about 6 g of glutamine per 100 g of amino acids. After two days, the patients of the control group are fed using a standard, enterally administered formula; initially using a nasogastric tube and then orally. The standard enteral formula contains less than about 8 g of glutamine per 100 g of amino acids. The patients of the test group are fed the nutritional composition of example 2 after two days. The patients receive about 2 liters of the formulas per day.

For all patients prior to surgery, the glutamine concentrations for intracellular skeletal muscle and plasma are substantially normal; about 10 to 15 μmol/g wet tissue and 0.6 mM/l respectively. After surgery, the glutamine concentrations drop; reaching values about one third less after two days. For the patients of the test group, the glutamine concentrations thereafter increase reaching substantially normal levels after about 12 days. The glutamine concentrations of the patients of the control groups remain reduced after 12 days.

The wounds of patients of the test group are determined to have healed to a much greater extent than those of the control group. Also the patients of the test group are sub-

jected to less weight loss after 12 days than the patients of the control group.

Example 4

A ready-to-drink nutritional composition is prepared. The nutritional composition includes the following components:

Component	Amount per liter	Energy %
Protein		25
Carob germoat bran:whey (61:25:14)		
Carbohydrate		45
Corn syrup solids		
Sucrose		
Lipids		30
Corn oil, Canola oil, Soy lecithin, Residual Milk fat Coconut oil (MCT's)		
Vitamins		
Vitamin A	4000 IU	
β-carotene	2.0 mg	
Vitamin D	400 IU	
Vitamin E	60 IU	
Thiamin	3.0 mg	
Pyridoxine	4.0 mg	
Biotin	400 μg	
Minerals		
Zinc	24 mg	
Copper	2.0 mg	
Magnesium	4.0 mg	
Selenium	100 μg	
Sodium	876 mg	
Potassium	1500 mg	
Chloride	1300 mg	

The nutritional composition has an energy density of 1500 kcal/l and a ratio of ω6 fatty acids to ω3 fatty acid of about 7:1. The nutritional composition has the following amino acid composition:

Amino acid	Amount (mg/g protein)	Percentage of FAO/WHO requirements for > 2 years
Ile	38.3	137%
Leu	74.3	113%
Lys	59.8	103%
Met	12.5	—
Cys	20.3	—
Met + Cys	32.8	131%
Phe	38.1	—
Tyr	35.9	—
Phe + Tyr	74.1	118%
Thr	42.6	125%
Trp	12.2	111%
Val	46.5	133%
Arg	96.7	—
His	24.7	130%
Ala	45.2	—
Asp	87.3	—
Glu + Gln	243.2	—
Gln	154.1	—
Gly	46.2	—
Pro	44.4	—
Ser	45.9	—

Therefore the nutritional composition fully meets the FAO/WHO recommendations for children over the age of 2 years. Further, the nutritional composition contains about 15 g/100 g of amino acids of glutamine and about 10 g/100 g of amino acids of arginine.

We claim:

1. A nutritional composition for providing glutamine, the composition being in a liquid concentrate or ready-to-drink liquid form and comprising: a protein source including carob protein and a source of cysteine.

2. A nutritional composition according to claim 1 which further comprises a carbohydrate source; and a lipid source.

3. A nutritional composition according to claim 2 in which the protein source provides about 10% to about 30% of the energy of the nutritional composition; the carbohydrate source provides about 35% to about 60% of the energy of the nutritional composition; and the lipid source provides about 20% to about 40% of the energy of the nutritional composition.

4. A nutritional composition according to claim 1 in which the carob protein is in the form of a protein isolate or hydrolysate.

5. A nutritional composition according to claim 1 in which the carob protein provides about 40% to about 90% by weight of the protein source.

6. A nutritional composition according to claim 5 which includes an additional source of methionine selected from the group consisting of casein, whey, soy, rice and oat bran protein, or mixtures thereof.

7. A nutritional composition according to claim 2 in which the lipid source comprises a mixture of medium chain triglycerides and long chain triglycerides.

8. A nutritional composition according to claim 7 in which the lipid source comprises at about 20% to about 80% by weight of medium chain triglycerides.

9. A nutritional composition according to claim 2 in which the lipid source has a polyunsaturated fatty acid omega-6 (n-6) to omega-3 (n-3) ratio of about 4:1 to about 15:1.

10. A nutritional composition according to claim 9 in which the omega-3 and omega-6 fatty acids provide less than about 10% of total energy.

11. A nutritional composition according to claim 1 further comprising a source of tryptophan.

12. A liquid nutritional composition for providing glutamine, the composition comprising a protein source including carob protein cysteine and an additional source of methionine.

13. A nutritional composition according to claim 12 in which the protein source includes at least 24 mg/g protein of methionine and cysteine.

14. A nutritional composition according to claim 13 in which the source of methionine and cysteine is at least one component chosen from the group consisting of whey and casein.

15. A nutritional composition according to claim 12 which further comprises a carbohydrate source; and a lipid source.

16. A nutritional composition according to claim 15 in which the protein source provides about 10% to about 30% of the energy of the nutritional composition; the carbohydrate source provides about 35% to about 60% of the energy of the nutritional composition; and the lipid source provides about 20% to about 40% of the energy of the nutritional composition.

17. A nutritional composition according to claim 12 further comprising a source of tryptophan.

18. A liquid nutritional composition for providing glutamine, the composition having a protein source comprising an isolate or hydrolysate of carob protein; cysteine and an additional source of methionine.

19. A nutritional composition according to claim 18 in which the protein source includes at least 24 mg/g protein of methionine and cysteine.

20. A nutritional composition according to claim 19 in which the source of methionine and cysteine is at least one component chosen from the group consisting of whey and casein.

21. A nutritional composition according to claim 18 which further comprises a carbohydrate source; and a lipid source.

22. A nutritional composition according to claim 21 in which the protein source provides about 10% to about 30% of the energy of the nutritional composition; the carbohydrate source provides about 35% to about 60% of the energy of the nutritional composition; and the lipid source provides about 20% to about 40% of the energy of the nutritional composition.

23. A nutritional composition according to claim 18 further comprising a source of tryptophan.

24. A method of providing glutamine to a human or animal, the method comprising enterally administering to a human or animal in need thereof an effective amount of a liquid nutritional composition having a protein source including carob protein.

25. A method according to claim 24 in which the protein source includes a source of ripteine and an additional source of methionine.

26. A method according to claim 24 in which the human or animal is a stressed patient.

27. A method according to claim 26 in which the patient is critically ill, or is suffering from sepsis, injury, burns, or inflammation, or is recovering from surgery.

28. A method of improving the immune function of a human or animal by providing glutamine and arginine to the patient, the method comprising enterally administering to the patient an effective amount of a liquid nutritional composition having a protein source including carob protein.

29. A method according to claim 28 in which the protein source includes a source of cypteine and an additional source of methionine.

30. A method of providing glutamine to patients suffering from injured or diseased intestines or to maintain the physiological functions of the intestine, the method comprising enterally administering to the patient an effective amount of a liquid nutritional composition having a protein source including carob protein.

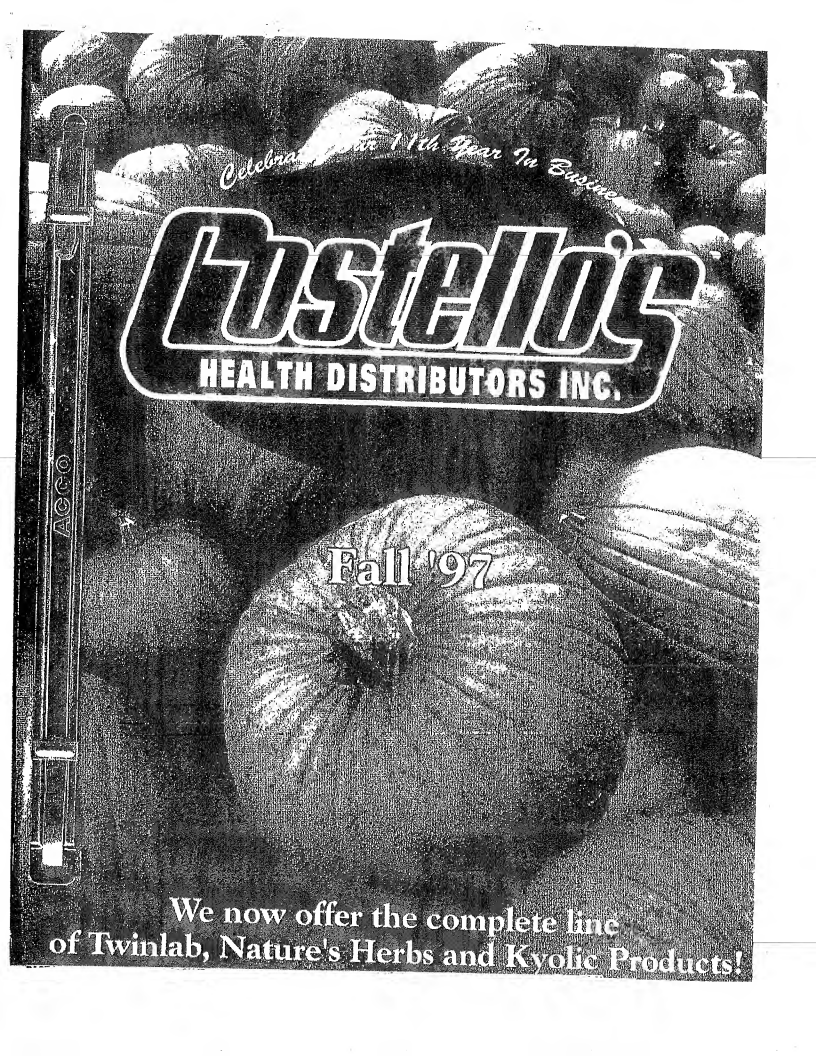
31. A method according to claim 30 in which the protein source includes a source of cysteine and an additional source of methionine.

32. A method of increasing plasma glutamine levels in a human or animal, the method comprising enterally administering to a human or animal in need thereof an effective amount of a liquid nutritional composition having a protein source including carob protein.

33. A method according to claim 32 in which the protein source includes a source of cysteine and an additional source of methionine.

* * * * *

EXHIBIT E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PROTEIN SUPPLEMENTS

Product Name	Size	Retail	Qty.	Total
[illegible]	12/box	1.19 ea.		
[illegible]	12/box	1.19 ea.		
[illegible]	12/box	1.59 ea.		
[illegible]	325 tabs	27.95		
[illegible]	32 oz.	21.95		

AMINO ACIDS

Product Name	Size	Retail	Qty.	Total
[illegible]	325 tabs	32.99		
[illegible]	160 tabs	17.99		
[illegible]	300's	39.99		
[illegible]	150's	19.50		
[illegible]	16 oz.	13.50		
[illegible]	32 oz.	22.95		
[illegible]	16 oz.	13.50		
[illegible]	32 oz.	22.95		
[illegible]	16 oz.	13.50		
[illegible]	32 oz.	22.95		
[illegible]	325 tabs	23.99		
[illegible]	160 tabs	12.99		
[illegible]	250 caps	29.99		
[illegible]	100 tabs	23.99		
[illegible]	90 tabs	21.99		
[illegible]	160 tabs	40.99		
[illegible]	90 tabs	16.99		
[illegible]	60 tabs	30.99		
[illegible]	30 caps	26.99		
[illegible]	30 caps	49.99		
[illegible]	12 fl. oz.	15.99		
[illegible]	150 gm.	21.99		
[illegible]	300 gm.	39.99		
[illegible]	60 caps	13.50		
[illegible]	120 caps	24.95		

ENERGY SUPPLEMENTS

Product Name	Size	Retail	Qty.	Total
[illegible]	3 lbs.	14.19		
[illegible] - Orange	3 lbs.	14.99		
[illegible] - Punch	3 lbs.	14.99		
[illegible] - Grape	3 lbs.	14.99		

PROTEIN POWDERS

Code	Product Name	Size	Retail	Qty.	Total
02 012	100% Instant Egg Protein Vanilla	1 lb.	19.99		
02 013	100% Instant Egg Protein Vanilla	2 lbs.	35.99		
02 175	100% Instant Egg Protein Vanilla	4 lbs.	65.99		
02 074	100% Instant Egg Protein Chocolate	1 lb.	19.99		
02 075	100% Instant Egg Protein Chocolate	2 lbs.	35.99		
02 176	100% Instant Egg Protein Chocolate	4 lbs.	65.99		
02 017	100% Instant Egg Protein Pineapple	1 lb.	19.99		
02 018	100% Instant Egg Protein Pineapple	2 lbs.	35.99		
02 171	100% Instant Egg Protein Banana	1 lb.	19.99		
02 172	100% Instant Egg Protein Banana	2 lbs.	35.99		
02 155	Egg D'Lite All Natural Egg Whites	1 lb.	19.99		
02 156	Egg D'Lite All Natural Egg Whites	2 lbs.	35.99		
02 019	ProComplex Vanilla	2.2 lbs.	37.99		
02 020	ProComplex Chocolate	2.2 lbs.	37.99		
02 027	ProComplex Strawberry	2.2 lbs.	37.99		
02 032	ProComplex All Natural Plain	2.2 lbs.	37.99		
02 149	ProComplex Vanilla	4.4 lbs.	70.99		
02 150	ProComplex Chocolate	4.4 lbs.	70.99		
02 151	ProComplex Strawberry	4.4 lbs.	70.99		
02 152	ProComplex All Natural Plain	4.4 lbs.	70.99		
02 030	100% Inst Ion Exchange Protein-Choc	2 lbs.	41.99		
02 031	100% Inst Ion Exchange Protein- Van	2 lbs.	41.99		
02 101	Super Pro 90 - Vanilla	1 lb.	9.29		
02 102	Super Pro 90 - Vanilla	2 lbs.	17.99		
02 103	Super Pro 90 - Chocolate	1 lb.	9.29		
02 104	Super Pro 90 - Chocolate	2 lbs.	17.99		
02 106	Superior M/E Protein - Vanilla	2 lbs.	24.99		
02 108	Superior M/E Protein - Chocolate	2 lbs.	24.99		
02 288	100% Whey Protein - Chocolate	2 lbs.	25.99		
02 289	100% Whey Protein - Vanilla	2 lbs.	25.99		

CREATINE SUPPLEMENTS

Code	Product Name	Size	Retail	Qty.	Total
† 02 167	Creatine 750 mg.	60 caps	5.99		
† 02 168	Creatine 750 mg.	120 caps	9.99		
† 02 133	Creatine 2500 Caps	100 caps	20.99		
† 02 134	Creatine 2500 Caps	200 caps	37.99		
† 02 135	Creatine 2500 Caps	300 caps	52.99		
† 02 201	Creatine Powder	150 grams	12.99		
† 02 202	Creatine Powder	300 grams	23.99		
† 02 204	Creatine Powder	600 grams	43.99		
† 02 216	Creatine Powder	1200 grams	78.99		
† 02 169	Pre-Load Creatine Complex-Punch	2 lbs.	19.99		
† 02 170	Pre-Load Creatine Complex-Orange	2 lbs.	19.99		
† 02 165	Pre-Load Creatine Complex-Grape	2 lbs.	19.99		
† 02 237	Pre-Load Creatine Complex-Punch	4 lbs.	33.99		
† 02 238	Pre-Load Creatine Complex-Orange	4 lbs.	33.99		
† 02 239	Pre-Load Creatine Complex-Grape	4lbs.	33.99		
† 02 240	Pre-Load Creatine Comp. Pun ind. Serv.	12/box	21.49/1.79ea.		
† 02 241	Pre Load Creatine Comp. Org Ind. Serv.	12/box	21.49/1.79ea.		
† 02 242	Pre-Load Creatine Comp. Grp Ind. Serv.	12/box	21.49/1.79ea.		

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3. ON's 100% Whey Protein now CONTAINS LACTASE and AMINOGEN™ digestive enzymes to further enhance absorption and make this product even more friendly to lactose intolerant individuals.

4. HIGHER PROTEIN PERCENTAGE. ON's 100% Whey Protein has always been a leader in this respect. With 23 grams of protein in just a one ounce serving, it's nearly 81% protein by weight!

5. ON's 100% Whey Protein is INSTANTIZED to mix easily and completely with just a few twirls of a spoon.

6. Every serving supplies even MORE low, moderate, and high molecular weight, biologically active WHEY PROTEIN MICROFRACTIONS including Alpha-lactalbumin, Glycomacropeptides, Beta-lactoglobulin, Immunoglobulin G (IgG), Lactoferrin, lactoperoxidase, and various growth factors.

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Whey MRP
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Cell Tech
Hydroxycut

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Supplement Facts

Serving Size 1 Scoop (29.4 g)

	Amount Per Serving	% Daily Value
Calories	110	
Calories from Fat	10	
Total Fat	1.5 g	2%*
Saturated Fat	0.5 g	3%*
Cholesterol	10 mg	4%*
Total Carbohydrate	3 g	1%*
Sugars	1 g	†
Protein	23 g	46%*
Calcium	150 mg	15%*
Sodium	40 mg	2%*
Potassium	220 mg	6%*
Enzyme Blend	10 mg	
Aminogen®		†
Lactase (standardized to 100,000 FCC units/g)		†

* Percent Daily Values are based on a 2,000 calorie diet.
† Daily Value not established.

Other Ingredients:
Protein Blend (Whey Protein Isolate, Whey Protein Concentrate, and Whey Peptides), Cocoa, Artificial Flavor, Lecithin, Acesulfame Potassium.

*Gold Standard Flavor has Whey Protein Isolates as the primary protein source.

Typical Amino Acid Profile per Scoop
Alanine: 1380 mg
Arginine: 480 mg
Aspartic Acid: 2490 mg
Cystine: 440 mg

Glutamine & Precursors: 3870 mg
Glycine: 530 mg
Histidine: 400 mg
Isoleucine: 1520 mg
Leucine: 2470 mg
Lysine: 2120 mg
Methionine: 440 mg
Phenylalanine: 670 mg
Proline: 1540 mg
Serine: 1240 mg
Threonine: 1720 mg
Tryptophan: 240 mg
Tyrosine: 590 mg
Valine: 1440 mg

Suggested Use:
As a dietary supplement, mix 1 heaping scoop of 100% Whey Protein with 4-8 ounces (depending on desired consistency) of water, skim milk or your favorite beverage. Consume 1-3 servings daily or use as recommended by a physician or licensed nutritionist.

Share your knowledge of this product with other customers... Be the first to write a review.

Browse for more products in the same category as this item:

Protein Powders > Whey Protein
Optimum Nutrition > Whey Protein
Protein Powders > Whey Protein > Whey Protein Large
Optimum Nutrition
Protein Powders

COMPARE PRODUCTS

100% Whey Protein 5 lbs by Optimum Nutrition **$29.95**

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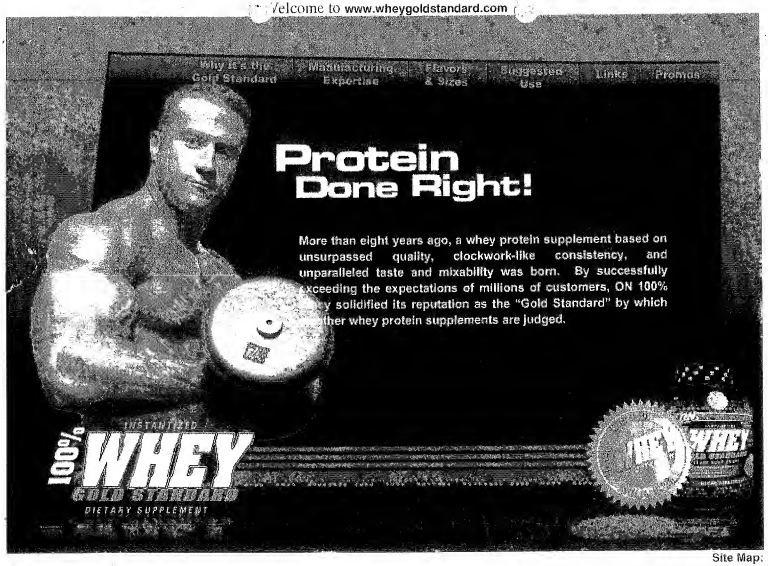

Site Map:

EXHIBIT F

BODY BUILDING.com

Optimum 100% Whey Protein

2 Lbs. ~~$23.00~~ **$13.98**
Extreme Milk Chocolate: [Order]
French Vanilla Creme: [Order]
Gold Standard Chocolate: [Order]
Gold Standard Chocolate Mint: [Order]
Gold Standard Cookies N' Cream: [Order]
Gold Standard Rocky Road: [Order]
Gold Standard Strawberry: [Order]
Gold Standard Tropical Punch: [Order]
Gold Standard Vanilla: [Order]

5 Lbs. ~~$43.00~~ **$28.89**
Extreme Milk Chocolate: [Order]
French Vanilla Creme: [Order]
Gold Standard Chocolate: [Order]
Gold Standard Chocolate Mint: [Order]
Gold Standard Cookies N' Cream: [Order]
Gold Standard Rocky Road: [Order]
Gold Standard Strawberry: [Order]
Gold Standard Tropical Punch: [Order]
Gold Standard Vanilla: [Order]

10 Lbs. ~~$79.00~~ **$55.79**
Gold Standard Chocolate: [Order]
Gold Standard Rocky Road: [Order]
Gold Standard Strawberry: [Order]
Gold Standard Vanilla:

Optimum Presents:
100% Whey Protein
With Faster-Acting HYDROWHEY!

Other Products

This works well with:
>Chitosan Plus
>Xylitol
>Lean Elite
>Mega L-Carnitine

Whey Protein Isolates As The Primary Protein Source!

Note: Optimum has made a slight change to the formula of 100% Whey Protein to make it an even better protein powder. The name is changing also to be "100% Whey Gold Standard". The price will remain the same though!

***Try the Extreme Milk Chocolate and French Vanilla Creme. These are Optimum's new Limited Edition Flavors.**

Supplement Of The Year [More Info]

Protein Powder Of The Year [More Info]

Optimum 100% Whey Protein won the Supplement Of The Year and Protein Powder Of The Year award for 2005 and 2006! Since the very beginning, Optimum Nutrition has raised the standard by which all other whey protein supplements are judged. Now we're raising the bar again with the 3rd generation of ON 100% Whey Protein: ON 100% Whey Gold Standard.

Like its predecessors, this canister of ON 100% Whey Gold Standard contains Optimum Nutrition's exclusive, propriotary blond of...

- Microfiltered Whey Protein Isolates
- Ion-Exchange Whey Protein Isolates
- Ultrafiltered Whey Protein Concentrate
- HydroWhey Hydrolyzed Whey Peptides

To give you more of what you want (pure, unadulterated whey protein) with less of what you don't (fat, saturated fat, cholesterol, lactose, and other carbohydrates) with every serving. This whey protein supplement is no exception. In fact, ON 100% Whey Gold Standard is better than ever! Here's why:

1. ON 100% Whey Gold Standard provides more whey protein isolates

[Order]

Other Optimum Products

About Optimum

What's In It?
Supplement Facts:

Container Size: 2 Lbs.
Serving Size: 1 Scoop
Servings Per Container: 31

Container Size: 5 Lbs.
Serving Size: 1 Scoop
Servings Per Container: 74

Container Size: 10 Lbs.
Serving Size: 1 Scoop
Servings Per Container: 155

Amount Per Serving:

Calories: 120
-Calories from Fat: 10
Total Fat: 1g
-Saturated Fat: 0.5g
Cholesterol: 30mg
Total Carbohydrates: 3g
-Sugars: 1g
Protein: 24g
Calcium: 140mg
Sodium: 60mg
Potassium: 220mg
Enzyme Blend: 25mg
-Aminogen --
-Lactase --

Other Ingredients:
Protein blend (whey protein isolate, whey protein concentrate, whey peptides), cocoa (processed with alkali), artifical flavor, lecithin, acesulfame potassium.

Note: Nutritional content and ingredients may vary slightly between flavors.

Directions: To encourage a positive nitrogen balance, consume approximately 1 gram of protein per pound of body weight per day from a combination of high protein foods and supplements. For even better results, consume your daily protein allotment over 4-6 small meals spread evenly throughout the day.

*Try the Extreme Milk Chocolate and French Vanilla Creme. These are Optimum's new Limited (WPI) - the purest and most expensive source of whey protein available.

2. Higher protein percentage. ON's 100% Whey Gold Standard has always been a leader in this respect. Now with 24 grams of protein in just slightly over one-ounce serving, it's nearly 79% protein by weight!

3. We've included more HydroWhey strategically hydrolyzed, low molecular weight whey peptides to make ON's 100% Whey Gold Standard even faster acting!

4. ON's 100% Whey Gold Standard now contains lactase and Aminogen digestive enzymes to further enhance absorption and make this product even more friendly to lactose intolerant individuals.

5. ON's 100% Whey Gold Standard is instantized to mix easily and completely with just a few twirls of a spoon.

6. Every serving supplies even more low, moderate, and high molecular weight, biologically active whey protein microfractions including Alpha-lactalbumin, Glycomacropeptides, Beta-lactoglobulin, Immunoglobulin G (IgG), Lactoferrin, lactoperoxidase, and various growth factors.

7. Over 4 grams of glutamine and glutamine precursors as well as 5 grams of BCAAs (leucine, isoleucine, and valine) in each scoop!

Order today using our 100% secure server and get it at the lowest prices in the world with our fast, inexpensive 2 - 3 day shipping! NOBODY beats our overall price!

2 Lbs. ~~$23.00~~ $13.98
Extreme Milk Chocolate: [Order]
French Vanilla Creme: [Order]
Gold Standard Chocolate: [Order]
Gold Standard Chocolate Mint: [Order]
Gold Standard Cookies N' Cream: [Order]
Gold Standard Rocky Road: [Order]
Gold Standard Strawberry: [Order]
Gold Standard Tropical Punch: [Order]
Gold Standard Vanilla: [Order]

5 Lbs. ~~$43.00~~ $28.89
Extreme Milk Chocolate: [Order]
French Vanilla Creme: [Order]
Gold Standard Chocolate: [Order]
Gold Standard Chocolate Mint: [Order]
Gold Standard Cookies N' Cream: [Order]
Gold Standard Rocky Road: [Order]
Gold Standard Strawberry: [Order]
Gold Standard Tropical Punch: [Order]
Gold Standard Vanilla: [Order]

10 Lbs. ~~$79.00~~ $55.79
Gold Standard Chocolate: [Order]
Gold Standard Rocky Road: [Order]
Gold Standard Strawberry: [Order]

Edition Flavors.	Gold Standard Vanilla: [Order]
Warnings: This product contains whey derived from dairy and lecithin (to improve mixability) derived from soybeans. For use as a dietary supplement only. Do not use for weight reduction.	**Learn more about Whey Protein.**
These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.	**Check out other Fat Loss Products.**